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An Ecofriendly Catalytic Route for the Preparation of Perfumery Grade Methyl Anthranilate from Anthranilic Acid and Methanol

G. D. Yadav* and M. S. Krishnan

Chemical Engineering Division, University Department of Chemical Technology, University of Mumbai, Matunga, Mumbai 400 019, India

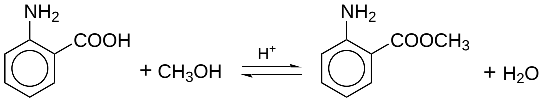
Abstract:

Methyl anthranilate is a very important perfumery ester and also a precursor to a number of Schiff bases which are used in several fragrance formulations. The current practice is to use homogeneous acids as catalysts in the manufacture of methyl anthranilate either starting with isatoic anhydride and methanol or by the esterification of anthranilic acid with methanol. These routes pose problems of disposal of liquid acids after the reaction, and substantial quantities of acids are required in order that the amine group be initially blocked as an amine hydrochloride. This paper deals with the application of ecofriendly heterogeneous catalysts including ZSM-5; acid-treated clays such as Filtrol-24 and K10; ion-exchange resins such as Nafion-H, Indion-130, Amberlyst-15, Amberlyst-18, Dowex M-32 and Bayer K-24; and dodecatungstophosphoric acid, a heteropolyacid. Among these catalysts, Amberlyst-15 and Indion-130 resins were found to be the most effective. Other heterogeneous catalysts such as ZSM-5, Filtrol-24, and dodecatungstophosphoric acid were found to be totally ineffective. A theoretical model was employed for the analysis of this solid-catalysed slurry reaction, and effects of various parameters on the rate of reaction were evaluated. There was no effect of external as well as internal mass-transfer resistance on the rate of reaction. The reaction was found to be intrinsically kinetically controlled, and the kinetic parameters were established. The product was isolated and confirmed by spectroscopic methods. The odour value matched with that of the commercially available perfumery grade sample.

Introduction

Organic esters are most frequently used as perfumery and flavour chemicals. They fall into a very wide category ranging from aliphatic to aromatic with various substitutions and multifunctional groups.[1,2] Most esters have pleasant odours reminiscent of floral to fruity notes. Methyl anthranilate is one such interesting ester which occurs naturally in several citrus fruits like orange and also in some flowers like neroli and ylang ylang. It finds more applications in flavouring than perfumery compositions because of its odour, which resembles the musky−fruity−dry floral note imitating concord grapes and orange blossom. It blends very well with several flavours and finds usage in the flavouring of soft drinks and alcoholic beverages. The annual production of methyl anthranilate was 186 tonnes (t)[3] in 1964 and is currently estimated to be over 1000 t. The major commercial routes are based on esterification of anthranilic acid with methanol or isatoic anhydride with methanol, and these employ homogeneous acid catalysts, posing problems of disposal.

Esterification is a very widely understood reaction especially in the pharmaceutical, perfumery, and flavour industry. Several synthetic routes exist to make esters, but most of them are not suitable to meet the stringent specifications applied in the perfumery and flavour industry. Yadav and Mehta[2] have reviewed these methods, including catalysis. The most acceptable method of making an ester is to react the corresponding acid with an alcohol.[4] The reaction is catalysed by acids and is reversible. Several methods are available to drive the reaction towards the favourable product. One of them is to use an excess amount of alcohol, and the other way is to remove the ester formed (or the coproduct water) continuously. The general reaction is as follows:



In the conventional industrial processes involving homogeneous acids, utilisation of heterogeneous acid catalysts as the replacement is gaining importance due to their ecofriendly nature.[5−8] These catalysts are noncorrosive and easy to separate from the reaction mixture. They can also be used repeatedly over a prolonged period without any difficulty in their handling and storage. Therefore the preparation of methyl anthranilate over various solid acid catalysts was undertaken including theoretical interpretation of collected data and modelling. The product was isolated to determine its perfume value. This paper reports these findings.

Preparation of Methyl Anthranilate

Reactions with sterically hindered compounds have always been a challenge regarding scale-up, selectivity, and separation. The preparation of methyl anthranilate is one

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* Author to whom correspondence should be addressed. Fax: 91-22-4145614. Tel: 91-22-4145616. E-mail: gdy@udct.ernet.in.

(1) Ogliaruso, M. A.; Wolfe J. F. *Synthesis of Carboxylic Acids, Esters and Their Derivatives*; John Wiley: New York, 1991.

(2) Yadav, G. D.; Mehta, P. *Ind. Eng. Chem. Res.* **1994**, *33* (9), 2198−2208.

(3) Bedoukian, P. Z. *Perfumery and Flavouring Synthesis*, 3rd ed.; Allured Publishing Corp.: Wheaton, IL, 1986.

(4) Carey, F. A. *Advanced Organic Chemistry*; 3rd ed.; Plenum Press: New York, 1990.

(5) Yadav, G. D.; Kirthivasan, N. *J. Chem. Soc., Chem. Commun.* **1995**, 203−204.

(6) Yadav, G. D.; Bokade, V. V. *Appl. Catal., A* **1996**, *147*, 299−323.

(7) Yadav, G. D.; Thorat, T. S. *Ind. Eng. Chem. Res.* **1996**, *35*, 721−732.

(8) Thorat, T. S.; Yadav, V. M.; Yadav, G. D. *Appl. Catal., A* **1992**, *90*, 73.

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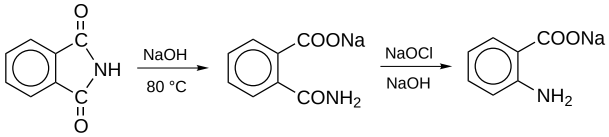
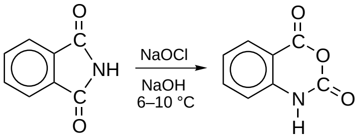
such reaction and involves the esterification of an ortho-substituted carboxylic acid. The reaction is known to occur with great difficulty. The earliest reports[3] mention that several process modifications were carried out by Walbanum in 1899 before an acceptable product having the desired perfumery grade could be synthesised. The process, however, achieved the GRAS (generally regarded as safe) status only in 1965.

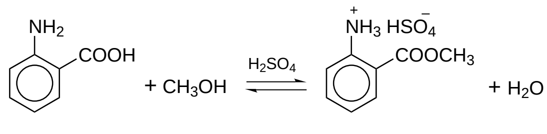
Certain anthranilates were known to exist as early as 1841 when Fritzche[9] discovered anthranilic acid while making indigo for the dyestuff industry. It would not be out of place here to mention briefly the preparation of anthranilic acid because the developments in making this chemical led to the synthesis of isatoic anhydride. It was later realised that isatoic anhydride is the most suitable compound for making perfumery grade methyl anthranilate. Anthranilic acid was made by reacting phthalimide with NaOCl in alkaline medium. The reaction was unknowingly overdone to make anthranilic acid as follows:



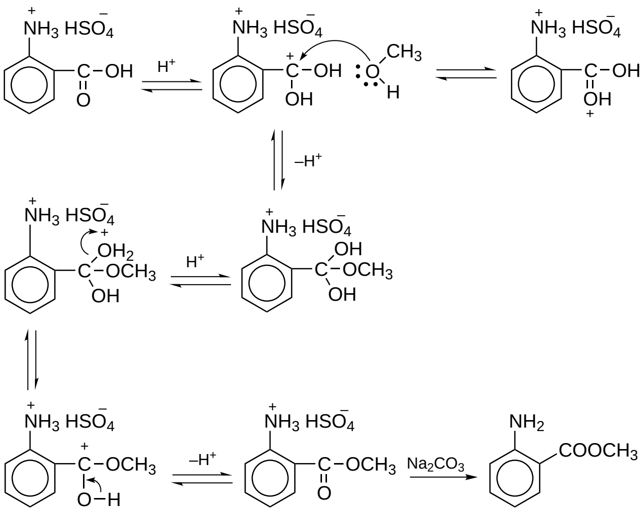
Isatoic anhydride, known to be the intermediate species formed in the reaction, was then isolated through a modified Hoffmann reaction. The reaction conditions were suitably monitored to give isatoic anhydride as follows:



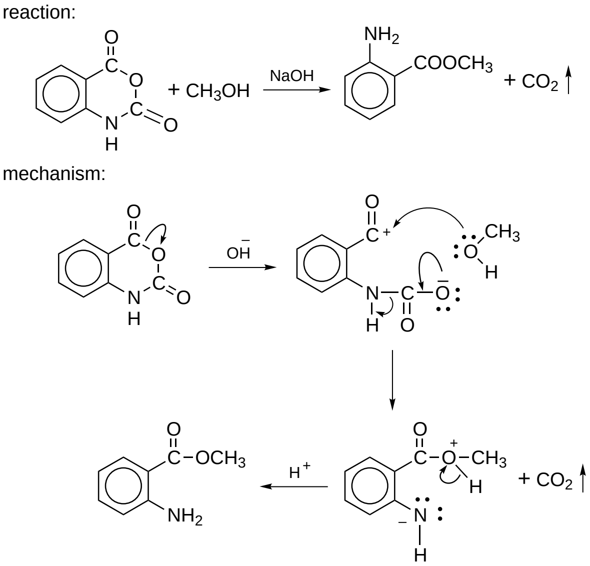
Anthranilic Acid Route. Esterification of anthranilic acid is extremely difficult owing to the presence of an ortho-substituted amine functionality. Since the reaction is acid-catalysed, large amounts of acid need to be used to prepare the salt of the amine, and then the salt is esterified with excess methanol. The product is treated with an alkali to neutralise the excess acid. The separated oily liquid is then vacuum distilled to give pure methyl anthranilate. The overall yield is relatively low. This method has to be employed very carefully because it can lead to charring and resin formation. Also the salt-formation step is very tricky, and proper care has to be taken to ensure the completion of salt formation. The sequence is represented as follows:



The reaction of methanol with anthranilic acid is rather straightforward and follows the normal esterification mechanism. The only problem is that it consumes large amounts of sulphuric acid and methanol. Once the ortho position of anthranilic acid is blocked through the sulphate salt, the remaining sulphuric acid acts as a catalyst for esterification. A large excess of methanol must be used in order to favour the transformation of the amino salt to make it suitable for the attack of the O atom from the alcohol, by way of which a carbocation is formed as shown in the reaction mechanism depicted. Blocking the amino group favours the preferential attack of the O atom first to the C$^+$ carbocation, which is more electronegative than N$^+$. However, the resin formation cannot be avoided effectively, and the yields are normally less than expected.



Isatoic Anhydride Route. Several patents have covered the preparation of methyl anthranilate from isatoic anhydride. Ramachandra[10] prepared methyl anthranilate through this method and found that the product was of the correct perfumery grade. The reaction mechanism is given as follows:



Staiger[11] prepared methyl anthranilate from methanol and isatoic anhydride in a long tube along with aqueous NaOH.

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[9] Fritzche, F. S. *J. Prakt. Chem.* **1841**, *23*, 67.

[10] Ramachandra, M.; Mahapatra, P. G. (to CSIR). Indian Patent 146359, 1988; *Chem. Abstr.* **1980**, *92*, 22281m.

[11] Staiger, W. K. *J. Org. Chem.* **1959**, *24*, 1214.

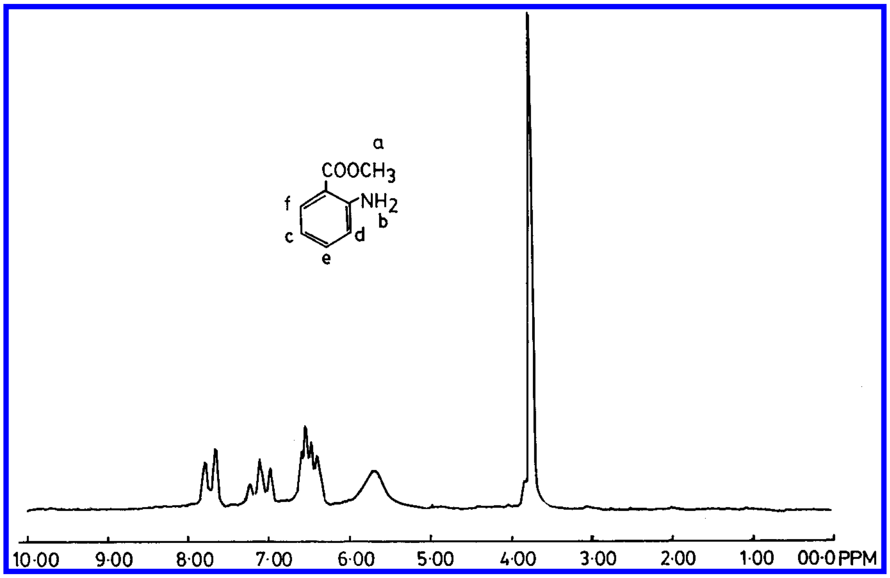

Figure 1. **^{1}H NMR spectra of methyl anthranilate: (a) 3.7 (3H, s), (b) 5.7 (2H, s), (c and d) 6.5 (2H, m), (e) 7.1 (1H, t), (f) 7.6 (1H, d).**

The yield was more than 95%. Several esters having the best perfumery characteristics are prepared by methods based on this one. However, the nonavailability of pure isatoic anhydride at competitive prices makes it unattractive as a starting material.

It is obvious that the anthranilic acid route could be adopted with heterogeneous catalysts. A systematic investigation of the esterification of anthranilic acid with methanol was therefore undertaken over a variety of solid acids such as ZSM-5; acid-treated clays such as Filtrol-24 and K10; ion-exchange resins such as Nafion-H, Indion-130, Amberlyst-15, Amberlyst-18, Amberlite-IR 120, Dowex M-32, and Bayer K-24; and dodecatungstophosphoric acid, a heteropolyacid (HPA).

Experimental Method

Chemicals and Catalysts. All chemicals and catalysts were procured from firms of repute: anthranilic acid (LR; Loba Chemie), methanol (AR; s.d. Fine Chem Ltd.), ZSM-5 (Associated Chemical Company, Mumbai), Filtrol-24 (Engelhart Inc.), K10 clay (Fluka), dodecatungstophosphoric acid (AR; s.d. Fine Chem Ltd), ion-exchange resins (IERs) such as Nafion-H (DuPont), Indion-130 (Ion Exchange Ltd), Amberlyst-15, Amberlyst-18 (Rohm and Haas), Amberlite-IR 120 (LR; s.d. Fine Chemical), Dowex M-32 (Dow Chemicals), and Bayer K-24 (Bayer).

Procedure. The reaction was carried out in a Parr autoclave of 100-mL capacity; 5 g of anthranilic acid, 50 mL of methanol, and 1.35 g of the particular catalyst were charged to the autoclave. The reaction mixture was allowed to reach the desired temperature, and the initial/zero time sample was collected. Agitation was then commenced at a known speed. Samples were withdrawn periodically for analysis. In most of the cases, methanol was taken in large molar excess over anthranilic acid to drive the equilibrium towards the ester formation. It was interesting to note that the reaction mixture developed an intense odour of methyl anthranilate as the reaction proceeded.

Analysis and Isolation of Product

The analysis was carried out by high-performance liquid chromatography (Tosoh, UV-8010) at ambient temperature. A Merck 50983 column with a stationary phase of Lichrospher 100 RP-18, particle size 5 μm, prepacked on a 250 × 4 mm i.d. column, with the Tosoh UV-8010 detector set at 254 nm, was used. The eluent used for analysis was an 80:20 methanol−water mixture with a flow rate of 0.8 mL/min. Pure samples of the reactants and products and their synthetic mixtures were used to calibrate the chromatograms.

For isolation of product, the catalyst was filtered off and the excess unreacted methanol was removed from the reaction mixture by rotovac. The remaining mass was treated with hexane, in which only the ester was extracted, leaving behind unreacted anthranilic acid. The hexane phase was treated with charcoal and filtered. The product was purified by distillation. It was confirmed by ^{1}H NMR (60 MHz Hitachi) and FTIR (Bruker IFS-88 single-channel Fourier transform spectrophotometer). The ^{1}H NMR spectrum is shown in Figure 1. Its odour was also evaluated vis-à-vis the pure commercial sample. The final product was a very pale yellow liquid with a dry odour resembling the odour of concord grapes and had a boiling point of 135 °C, matching the reported value.

Theoretical Aspects of Solid-Catalysed Liquid-Phase Reactions

The solid-acid-catalysed esterification is a typical solid−liquid slurry reaction for which some theoretical work has emanated from this laboratory.[12] The theory takes into account the evaluation of the intrinsic kinetics of the reaction.

The esterification reaction involves two organic-phase reactants, A (anthranilic acid) and B (methanol); and the desired product E (methyl anthranilate) and W (coproduct water):

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[12] Kumbhar, P. S.; Yadav, G. D. *Chem. Eng. Sci.* **1989**, *44* (11), 2535.

$$A + B \xrightarrow[\text{catalyst}]{\text{acid}} E + W \qquad (1)$$

Although A and B are liquid-phase reactants, they need to diffuse to the interior surface of the catalyst. The different steps involved in this process are as follows: (1) diffusion of A from bulk liquid phase to the exterior of the catalyst surface through the liquid film surrounding the catalyst particle (reflected in k_{SL-A}, solid–liquid mass transfer coefficient for A); (2) diffusion of B from the bulk liquid phase to the exterior of the catalyst surface through the liquid film surrounding the catalyst particle (reflected in k_{SL-B}, solid–liquid mass transfer coefficient for B); (3) intraparticle diffusion of A and B within the catalyst pores (reflected in the effectiveness factor, η); (4) adsorption of A and B on the catalyst surface (reflected in the adsorption equilibrium constants K_A and K_B); (5) reaction between adsorbed A and B to produce E and W according to a Langmuir–Hinshelwood mechanism; (6) desorption of E and W from the catalyst surface to the exterior of the catalyst; (7) transport of desorbed E and W to the bulk liquid phase.

Figure 2 shows the various cases that are likely to be encountered in a solid–liquid slurry reaction where the liquid-phase species A and B have to diffuse to the catalyst sites for reaction. Some pertinent equations are presented herein along with the concentration profiles of the reactants in the reaction mixture. At steady state the rate of mass transfer per unit volume of the liquid phase can be given by

$$R_A\ [\text{gmol/(cm}^3\cdot\text{s)}] = k_{SL-A}a_P\{[A_0] - [A_S]\} \qquad (2)$$

= rate of diffusion of A from the bulk liquid phase to the catalyst surface

$$= zk_{SL-B}a_P\{[B_0] - [B_S]\} \qquad (3)$$

= rate of diffusion of B from the bulk liquid phase to the catalyst surface

$$= \eta k_{R2}w[A_S][B_S] \qquad (4)$$

= rate of surface reaction per unit volume in the presence of intraparticle diffusion

where k_{R2} is the second-order rate constant, (cm^3/gmol)(cm^3/g)(1/s), a_P the external surface area per unit liquid volume (cm^2/cm^3), z the stoichiometric coefficient of reactant B per mole of reactant A, and w the catalyst loading per unit liquid volume (g/cm^3).

Eliminating the unknown surface concentrations of the reactants, $[A_S]$ and $[B_S]$, a quadratic equation in R_A is obtained. Equation 4 is a power-law model. When the adsorption and/or the desorption steps are likely to be important, eq 4 can be replaced by the Langmuir–Hinshelwood type of model invoking adsorption constants and fractional coverage of sites by the reactants.

When the surface reaction is very rapid with respect to the diffusion of either A and B or of A alone, several interesting cases emerge depending on the concentration of A and B in the liquid phase. The current investigation of reactions presented in this paper deals with a situation where the surface reaction was much slower than the diffusional steps, and thus the following equations are relevant; that is, if

$$\frac{1}{\eta k_{R2}w[A_0][B_0]} \gg \frac{1}{k_{SL-A}a_P[A_0]} \quad \text{and} \quad \frac{1}{k_{SL-B}a_P[B_0]} \qquad (5)$$

then the surface reaction is the controlling mechanism and the overall rate of the reaction will be the same as given by the surface reaction, that is,

$$R_A = \eta k_{R2}w[A_0][B_0] \qquad (6)$$

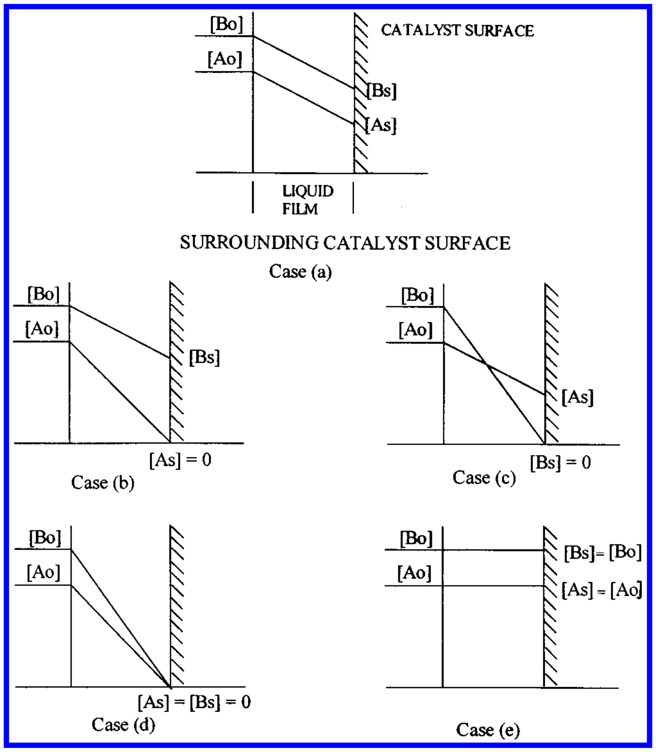

Figure 2. **Different concentration profiles around the catalyst particle for solid–liquid mass transfer (the particle may or may not be porous). (a) Both A and B encounter resistance by the liquid film surrounding the particles. (b) Both A and B encounter the resistance, and the concentration of A drops to zero on the surface of the particle. (c) Both A and B encounter the resistance, and the concentration of B drops to zero on the surface of the particle. (d) Both A and B encounter the resistance, and their concentrations drop to zero on the surface of the particle. (e) External resistance to solid–liquid mass transfer is absent.**

The influence of intraparticle diffusion, reflected in the effectiveness factor, can be studied by varying the particle size and also through the reaction temperature.

In order to discern the controlling mechanism, it was desirable to study the effect of various parameters on the overall rate of reaction.

Since one of the components is always taken as the limiting reactant, its concentration may not be uniform within the catalyst particle due to intraparticle diffusional resistance in contrast to that of the component used in excess. To account for this resistance, differential equations for intraparticle diffusion with reaction on the surface of the catalyst need to be solved, and problems of this type are well-known.[13] For a first-order reaction occurring in a spherical particle of radius R, one can relate the concentration of the limiting

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(13) Doraiswamy, L. K.; Sharma, M. M. *Heterogeneous Reactions, Analysis, Examples and Reactor Design*; John Wiley: New York, 1984; Vol. 2.

reactant at any radial distance r from the centre of the catalyst to its concentration on the surface by the equation

$$\frac{[\mathrm{A}]}{[\mathrm{A_S}]} = \frac{\sinh(3\phi r/R)}{[(r/R)]\,\sinh(3\phi)} \qquad (7)$$

where

$$\phi = \text{Thiele modulus} = (R/3)(\rho_\mathrm{P} k_\mathrm{R1}/D_\mathrm{e})^{1/2} \qquad (8)$$

$$k_\mathrm{R1} = k_\mathrm{R2}[\mathrm{B_0}] \qquad (9)$$

where k_R1 is the pseudo-first-order rate constant, in (cm^3/g)(1/s), D_e is the effective diffusivity of A in the pores (cm^2/s), and ρ_P is the particle density (g/cm^3).

It is desirable to express the effect of intraparticle diffusion in terms of the effectiveness factor η:

$$\eta = (1/\phi)[\coth 3\phi - 1/(3\phi)] \qquad (10)$$

Equation 4 will now be rewritten as

$$R_\mathrm{A} = \eta k_\mathrm{R1} w[\mathrm{A_S}] \qquad (11)$$

Once again the concentration [A$_\mathrm{S}$] can be eliminated to get R_A as

$$R_\mathrm{A} = [\mathrm{A_0}]\{\rho_\mathrm{P} d_\mathrm{P}/(6k_\mathrm{SL-A} w) + 1/(\eta k_\mathrm{R1} w)\}^{-1} \qquad (12)$$

because

$$a_\mathrm{P} = 6w/(\rho_\mathrm{P} d_\mathrm{P}) \qquad (13)$$

$$R_\mathrm{A} = [\mathrm{A_0}]w\{\rho_\mathrm{P} d_\mathrm{P}/(6k_\mathrm{SL-A}) + 1/(\eta k_\mathrm{RI})\}^{-1} \qquad (14)$$

where d_P is particle diameter (cm).

Depending on the relative magnitudes of $k_\mathrm{SL-A}$ and k_R1, the controlling resistance can be determined.

In the absence of both external and internal resistance to mass transfer, it is possible to determine the intrinsic kinetics. Accordingly, for a pseudo-first-order reaction,

$$-\mathrm{d}[\mathrm{A_0}]/\mathrm{d}t = k_\mathrm{R1} w[\mathrm{A_0}] \qquad (15)$$

$$-\mathrm{d}[\mathrm{A_0}]/\mathrm{d}t = k_1[\mathrm{A_0}] \qquad (16)$$

where

$$k_1 = k_\mathrm{R1} w \qquad (17)$$

Integrating eq 16, the following is obtained:

$$-\ln([\mathrm{A_0}]/[\mathrm{A_0}]_i) = k_1 t \qquad (18)$$

or

$$-\ln(1 - X_\mathrm{A}) = k_1 t \qquad (19)$$

where X_A is the fractional conversion of A given as follows:

$$X_\mathrm{A} = ([\mathrm{A_0}]_i - [\mathrm{A_0}])/[\mathrm{A_0}]_i \qquad (20)$$

where subscript i refers to zero time concentration.

Thus a plot of $-\ln(1 - X_\mathrm{A})$ against time t will give slope, which represents k_1 and from which k_R1 can be determined. The above theory is developed for a single liquid phase containing the reactants, the products, and the solid catalyst. The water of reaction was miscible in the organic phase in the presence of methanol. When there is a multiphase system such as L−L−S, the diffusion of one of the reactants into the other liquid phase, which acts as a continuous phase and contains the catalyst, needs to be considered.

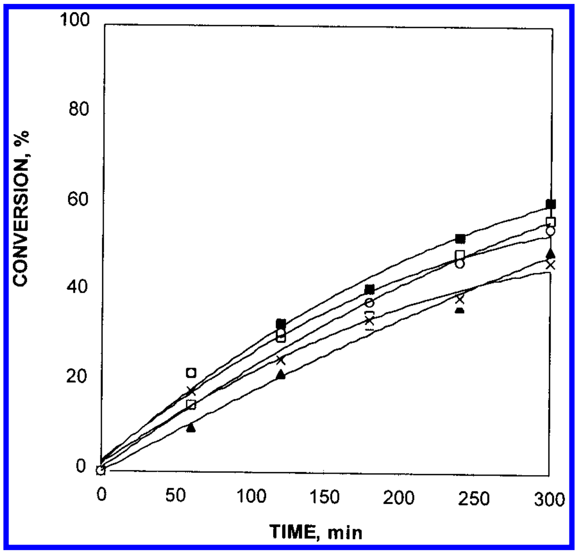

Figure 3. **Effect of different catalysts on the conversion of anthranilic acid: catalyst loading, 3.0% (w/w); particle size, 700 μm; temperature, 120 °C; speed of agitation, 1000 rpm; anthranilic acid, 5 g; MeOH, 50 mL. □, Indion-130; ■, Amberlyst-15; ▲, Amberlyst-18; ×, Dowex M-32; ○, Bayer K-24.**

Results and Discussion

Methanol was always taken in far excess, as mentioned earlier, over anthranilic acid, and the preliminary experiments were conducted under otherwise similar conditions of reactant concentration (or mole ratio), catalyst loading, particle size, speed of agitation, and temperature except the type of catalyst. It should be realised that the excess volume of methanol helps in driving the equilibrium to the right as well as dissolving anthranilic acid, which has a solubility of 0.107 g/cm^3 of methanol at 9.6 °C. Besides, it can be recycled without much difficulty. The solubility limitation notwithstanding, it is also possible to take lower mole ratios of methanol to anthranilic acid, keeping the alcohol phase always saturated with the acid at the reaction temperature. In order to eliminate errors in the analysis of data, the reaction was conducted with excess molar ratios.

Efficacy of Various Catalysts. Different solid acid catalysts were used to assess their efficacy in this reaction as mentioned earlier.

A 3.0% w/w loading of catalyst based on the organic mass of the reaction mixture was employed at a mole ratio of methanol to anthranilic acid of 34:1 at 120 °C and an agitational speed of 1000 rpm. It was expected to have no influence of external and/or internal resistance to mass transfer so that a comparative study based on intrinsic kinetics could be made. Further, as will be explained later, indeed there was no influence of mass transfer on the rate of reaction of anthranilic acid with methanol. Figure 3 shows plots of

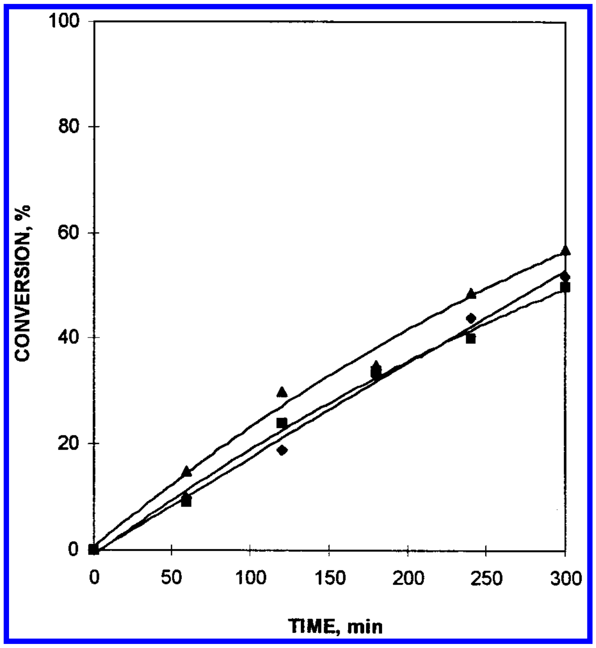

Figure 4. **Effect of the speed of agitation on the conversion of anthranilic acid: catalyst, Indion-130 (3.0% w/w); temperature, 120 °C; particle size, 700 μm; anthranilic acid, 5 g; MeOH, 50 mL; ◆, 1000 rpm; ■, 800 rpm; ▲, 500 rpm.**

the conversion of anthranilic acid, the limiting reactant, against time for the various catalysts.

It was found that the cation-exchange resins Amberlyst-15 and Indion-130 showed higher conversions compared to the other catalysts. Further experiments were conducted with Indion-130 as the catalyst, where only one parameter was varied at a time under otherwise similar experimental conditions. The choice of Indion-130 was based on its availability in the local market at much cheaper rates than Amberlyst-15.

Effect of Speed of Agitation. The speed of agitation was varied between 500 and 1000 rpm, and it was found that the conversions of anthranilic acid were unaffected by the speed in the range 500−1000 rpm. (Figure 4). Therefore, further experiments were conducted at or beyond 1000 rpm, to be on the safer side. Since alcohol B was chosen in far excess, there is a possibility of diffusional resistance for transfer of anthranilic acid A through the liquid film around the catalyst and then inside the pores. According to the model used for this analysis, the liquid-phase diffusivity values D_{AB} (anthranilic acid in methanol) and D_{BA} (methanol in anthranilic acid) were required, and these values were calculated by using the Wilke−Chang equation.[14] The value of D_{AB}, diffusivity of A in B at 120 °C, was calculated as 6.5×10^{-5} cm²/s.

The values of solid−liquid mass transfer coefficients k_{SL-A} were calculated by assuming the Sherwood number, $Sh = (k_{SL}d_P)/D = 2$, where D is the diffusivity. It should be noted that the actual Sherwood number could be much higher but, for orders of magnitude calculation, it is safe to take the lowest Sherwood number. Thus, k_{SL-A} was found as 1.857×10^{-3} cm/s for a particle size of Indion-130 of 0.07 cm.

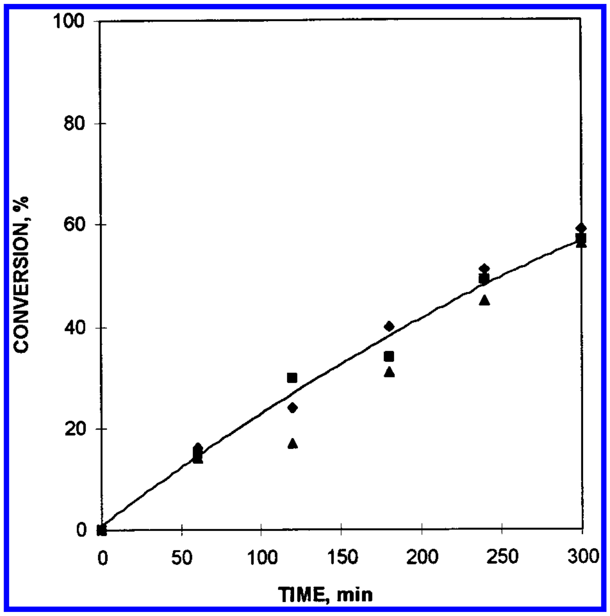

Figure 5. **Effect of the catalyst particle size on the conversion of anthranilic acid: catalyst, Indion-130 (3.0%); particle size, 700 μm; temperature, 120 °C; speed of agitation, 1000 rpm; anthranilic acid, 5 g; MeOH, 50 mL; ◆ 425−500 μm; ■, 600−850 μm; ▲ >850 μm.**

The value of a_P, particle surface area per unit liquid volume, was calculated from

$$a_P = \left[\frac{6w}{(\rho_P d_P)}\right] = 1.417\ \text{cm}^{-1}$$

Thus,

$$k_{SL-A}a_P[A_0] = 1.7628 \times 10^{-6}\ \text{gmol cm}^{-1}\ \text{s}^{-1}$$

and

$$k_{SL-A}a_P[B_0] = 4.9000 \times 10^{-7}\ \text{gmol cm}^{-1}\ \text{s}^{-1}$$

Thus, a typical initial rate of reaction was calculated as 2.789×10^{-8} gmol/(cm³ s). Therefore,

$$\frac{1}{\eta k_{R2} w[A_0][B_0]} \gg \frac{1}{k_{SL-A}a_P[A_0]} \quad \text{and} \quad \frac{1}{k_{SL-B}a_P[B_0]} \tag{21}$$

that is,

$$3.587 \times 10^{7} \gg 5.67 \times 10^{5} \quad \text{and} \quad 2.04 \times 10^{6}$$

The above inequality demonstrates that there is an absence of resistance due to the solid−liquid external mass transfer, and the rate may be either surface reaction controlled or intraparticle diffusion controlled.

Effect of Intraparticle Diffusion. The effect of intraparticle diffusional resistance was studied by taking three different particle size ranges as shown in Figure 5. For an average particle size less than 700 μm, there was no effect of particle size on the conversion of anthranilic acid. This would suggest that the effectiveness factor for this reaction is almost unity. As will be shown later, the effectiveness factor was indeed unity. Thus, there is no intraparticle diffusion and the entire process becomes surface reaction

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(14) Reid, R. C.; Prausnitz J. M.; Sherwood T. K. The Properties of Gases and Liquids, 3rd ed.; McGraw-Hill: New York, 1977.

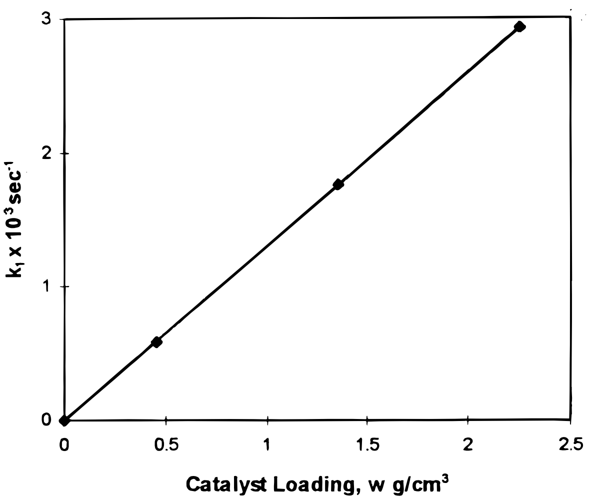

Figure 6. **Plot of the pseudo rate constant, k_1, versus catalyst loading, *w* (g/cm^3), on the conversion of anthranilic acid: catalyst, Indion-130; temperature, 120 °C; particle size, 700 μm; speed of agitation, 1000 rpm; anthranilic acid, 5 g; MeOH, 50 mL.**

controlled, where the chemisorbed A reacts with chemisorbed B on the interior surface of the particle. The percent of active sites on the exterior surface of particles is negligible. This was further confirmed by studying the effect of temperature on the rate of reaction, which gives the energy of activation.

Effect of Catalyst Loading. As per eq 6, in the absence of mass-transfer resistance, the rate of reaction is directly proportional to catalyst loading based on the entire liquid-phase volume. The catalyst loading was varied from 1% to 5% w/w of anthranilic acid, which corresponds to a *w* of 0.0083−0.0413 g/cm^3.

Either the initial rate of reaction or the pseudo rate constant k_1 could be plotted against *w*. It is seen that the rate is linearly proportional to *w* (Figure 6). More appropriately,

$$k_{SL-A}a_P\,\{[A_0]-[A_S]\} = \eta k_{R1} w[A_S] \tag{22}$$

but

$$a_P = \frac{6w}{\rho_P d_P} \quad \text{and} \quad \frac{k_{SL-A}d_P}{D_{AB}} = 2 \tag{23}$$

For $\eta = 1$,

$$\frac{[A_0]}{[A_S]} = 1 + \frac{k_{R1}\rho_P {d_P}^2}{12D_{AB}} \tag{24}$$

When intraparticle diffusion is present,

$$\phi = \frac{d_P}{6}\left[\frac{k_{R1}\rho_P}{D_{e-AB}}\right]^{1/2} \quad \text{and} \quad \eta = 1/\phi \tag{25}$$

where

$$D_{e-AB} = D_{AB}\epsilon/\tau \tag{26}$$

$$\frac{[A_0]}{[A_S]} = 1 + \left[\sqrt{\frac{k_{R1}D_{AB}\epsilon\rho_P}{\tau}}\right]d_P \tag{27}$$

where $\in$ = porosity, τ = tortuosity, and D_{AB} = bulk diffusivity of A in B.

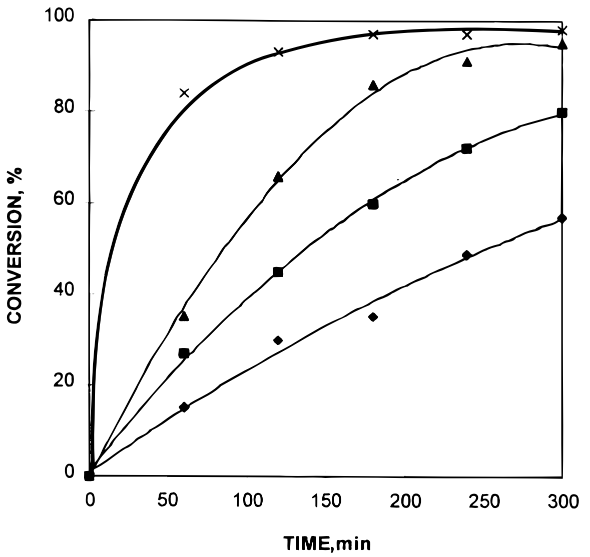

Figure 7. **Effect of concentration/mole ratio on the conversion of anthranilic acid: catalyst, Indion (3.0%); temperature, 120 °C; speed of agitation, 1000 rpm; particle size, 700 μm.**

symbol	initial mole ratio of anthranilic acid to MeOH	$[A_0]_i \times 10^4$, gmol/cm^3
◆	1:34	6.695
■	1:47	5.021
▲	1:72	3.347
×	1:148	1.674

Thus putting the appropriate values, it is seen that eq 24 is valid, giving $[A_0] \approx [A_S]$, that is, the rate is linearly proportional to catalyst loading in the absence of any intraparticle diffusion (Figure 6).

Effect of Mole Ratio. The concentration of methanol had an influence on the reaction rate and on the conversion. The rate of reaction is linear in the concentration of methanol. The mole ratio of anthranilic acid to methanol was varied from 1:34 to 1:136, and it was found that the conversion is very low at smaller mole ratios and that it is maximum at higher mole ratios. Beyond 1:136 there was no effect, and the reaction produced almost the same conversions (Figure 7).

Kinetics of the Reaction. When both external and internal mass-transfer resistances are absent, the kinetics of the surface reaction by using the power law model can be established.

When the molar ratio *M* of anthranilic acid to methanol is 1:1, eq 6 is integrated to get

$$\frac{X_A}{1-X_A} = [A_0]_i k_{R2} wt \tag{28}$$

By making a plot of $X_A/(1-X_A)$ versus *t*, we get a straight line whose slope represents k_{R2}. When $M \neq 1$, the integration of the above equation leads to the following equation:

$$\ln\left[\frac{M-X_A}{M(1-X_A)}\right] = [A_0]_i(M-1)k_{R2}wt \tag{29}$$

Thus, plots can be made of the left-hand-side term of eq 29 against time to determine k_{R2} which has the following

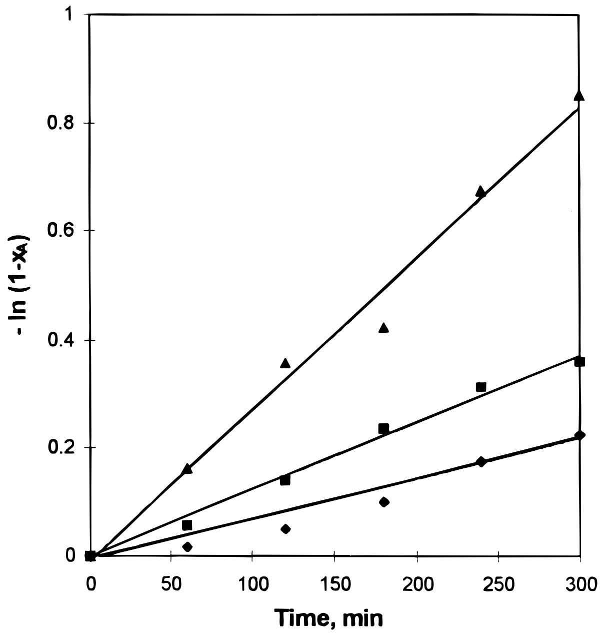

Figure 8. **Typical first-order plot for the reaction of anthranilic acid: catalyst, Indion-130 (3.0% w/w); speed of agitation, 1000 rpm; particle size, 700 μm; anthranilic acid, 5 g; MeOH, 50 mL; ◆, 100 °C; ■, 110 °C; ▲, 120 °C.**

units: (cm^3/gmol)(cm^3/g cat)(1/s). When M is very high, the rate constant k_{R1} is a pseudo constant.

$$k_{R1} = k_{R2}[B_0] \tag{30}$$

The integration of the relevant equation leads to

$$-\ln(1 - X_A) = k_1 t \tag{31}$$

where

$$k_1 = k_{R1}w = k_{R2}[B_0]w \tag{32}$$

In the present case plots were made of $-\ln(1 - X_A)$ versus t to determine k_1, from which k_{R1} and hence k_{R2} were calculated. Figure 8 shows this plot.

Effect of Temperature. The effect of temperature on conversion under otherwise similar conditions was studied in the range 100−120 °C as shown in Figure 9. It is seen that the conversion increases with temperature. The plots of $-\ln(1 - X_A)$ versus time indicate a straight-line behaviour typical of a pseudo-first-order reaction (Figure 8) . The rate constants k_1 at 100, 110, and 120 °C were 0.8×10^{-3}, 1.2×10^{-3}, and 2.8×10^{-3} s^{-1}, respectively from which k_{R2} values were calculated. The Arrhenius plot is shown in Figure 10, wherein ln k_{R2} is plotted against $1/T$ to get the activation energy as 18.176 kcal/gmol, which confirms that the reaction is intrinsically kinetically controlled.

Activity of Various Catalysts and Their Reusability. The activity of the various catalysts is evaluated on the basis of the second-order rate constants (k_{R2}) that are obtained under the kinetically controlled mechanism. Table 1 shows the values of k_{R2} for various catalysts. The activity of the catalysts is as follows: Amberlyst-15 > Indion-130 > Bayer K-24 > Amberlyst-18 > Dowex M-32.

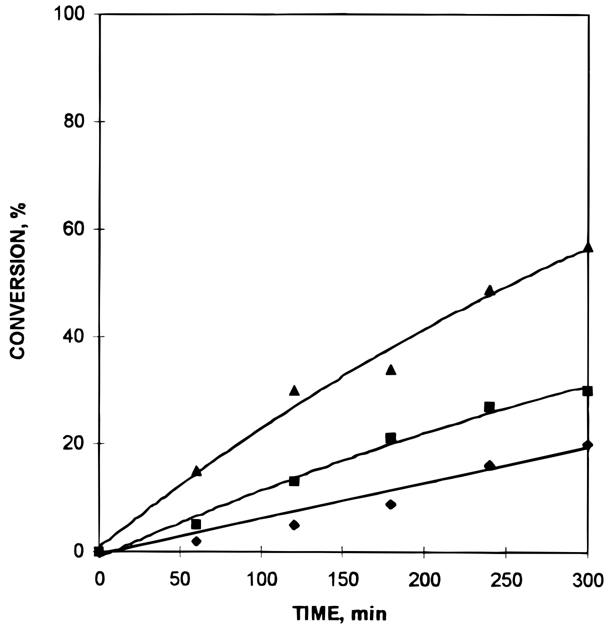

Figure 9. **Effect of temperature on the conversion of anthranilic acid: catalyst, Indion-130 (3.0% w/w); speed of agitation, 1000 rpm; particle size, 700 μm; anthranilic acid, 5 g; MeOH, 50 mL; ◆, 100 °C; ■, 110 °C; ▲, 120 °C.**

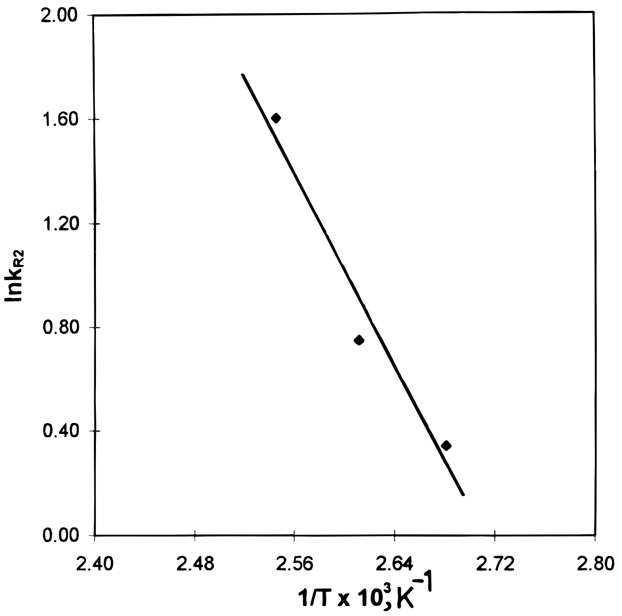

Figure 10. **Arrhenius plot of ln k_{R2} versus $1/T$: catalyst, Indion-130 (3.0% w/w); speed of agitation, 1000 rpm; particle size, 700 μm; anthranilic acid, 5 g; MeOH, 50 mL.**

The conventional inorganic catalysts like H-ZSM-5, acid-treated clays Filtrol-24 and K10, and a heteropolyacid (dodecatungstophosphoric acid, a homogeneous catalyst) did not show any activity for this reaction. These catalysts are well-known for their sensitivity towards aqueous conditions, and that might have caused their deactivation. The source for water would be the dehydration of methanol in the presence of acid catalysts and its formation as the by-product of this reaction. The inactivity of the above catalysts may also be due to the strong affinity of the $-NH_2$ group in anthranilic acid with the acidic centres of the catalysts. The

Table 1. **Rate constants for various ion exchange resin catalysts in the preparation of methyl anthranilate**

catalyst	k_{R2}, (cm^3/g)(cm^3/gmol)(1/s)
Amberlyst-15	5.28
Indion-130	4.93
Bayer K-24	4.41
Amberlyst-18	3.84
Dowex M-32	3.71

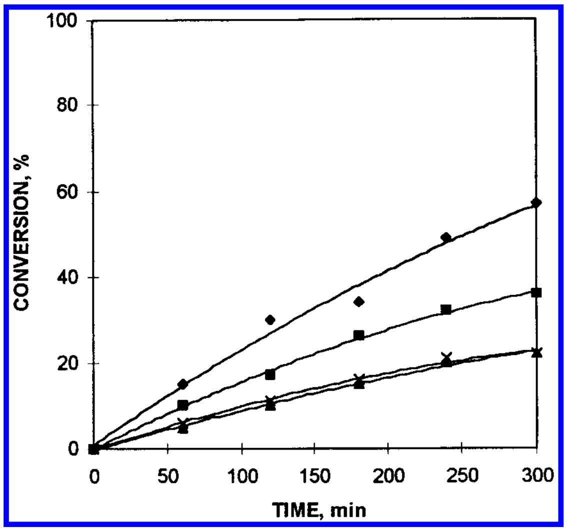

Figure 11. **Effect of catalyst reusability (without MeOH wash) on the conversion of anthranilic acid: catalyst, Indion-130 (3.0%); temperature, 120 °C; speed of agitation, 1000 rpm; particle size, 700 μm; anthranilic acid, 5 g; MeOH, 50 mL; ◆, fresh use; ■, first reuse; ▲, second reuse; ×, third reuse (MeOH washed).**

other ion-exchange resins Nafion-H and Amberlite-IR 120 have tighter pore structure vis-à-vis others as well as being highly acidic; it appears that bonding with $-NH_2$ groups is stronger, which poisons the useful acidity.

IER catalysts do not degrade or get affected by the water generated during the esterification because of their hydrophobic nature. It is speculated that some sites are blocked by adsorption of the $-NH_2$ end of anthranilic acid by complex formation with H^+ on the catalyst surface while the esterification occurs at the other group on the adjacent sites. The relative rates of adsorption of the anthranilic acid molecule by the above said mechanism on different catalysts determine the relative activity of the catalyst.

With reference to the acidity of these solid catalysts, the activity for esterification and the acidity do not show any trend. There is thus a distribution of available acidic sites amongst the $-NH_2$ and the $-COO-$ groups of the same molecule because of which not all sites of the catalyst are available for adsorption.

The catalyst was employed as such without any post-treatment/washings for three runs as shown in Figure 11. It was found that the activity had decreased with each use but the subsequent reduction in activity was marginal. Thus after the third use, the catalyst was washed with methanol to see that the same activity was maintained at the end of the fourth use.

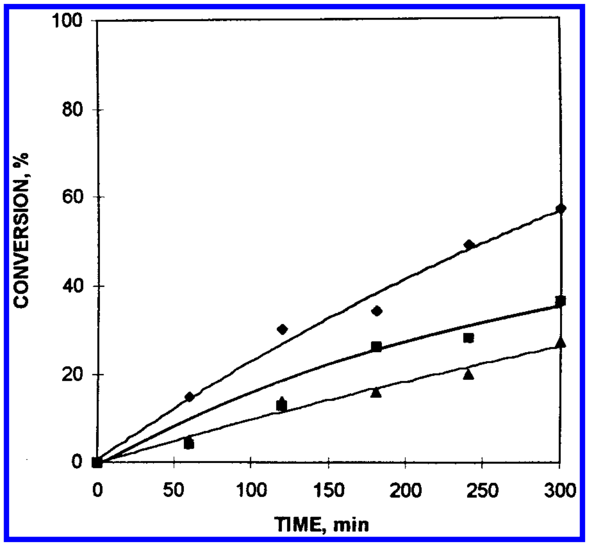

Figure 12. **Effect of catalyst reusability (without MeOH wash) on the conversion of anthranilic acid: catalyst, Indion-130 (3.0% w/w); particle size, 700 μm; temperature, 120 °C; speed of agitation, 1000 rpm; anthranilic acid, 5 g; MeOH, 50 mL; ◆, fresh use; ■, first reuse; ▲, second reuse.**

Therefore, a fresh set of experiments were conducted, wherein the catalyst was washed after each use. Figure 12 shows the results. There was a reduction in activity from the first use to the third use, but it appears that the decrease was marginal in the first run and the third run.

Odour Evaluation

The odour evaluation for the sample was performed, and it matched with the commercial sample. It was described as a sweet odour resembling the odour of dry concord grapes. Since there was no by-product formation with solid acid catalysts, almost all catalysts had similar olfactory values.

Conclusions

The current work has addressed the use a of variety of ecofriendly solid acid catalysts in the synthesis of methyl anthranilate from anthranilic acid and methanol. The ion exchange resin (IER) catalysts were found to be equally effective and highly selective except Nafion-H and Amberlite-IR 120. The conventional inorganic acid catalysts such as H-ZSM-5, acid-treated clays Filtrol-24 and K10, dodecatungstophosphoric acid (unsupported or supported on K10) did not show any activity to this reaction. The reaction requires catalysts of a hydrophobic nature such as IERs because the catalysts with the hydrophilic surface deactivate rapidly in the presence of water formed during the reaction. The overall rate of reaction is intrinsically kinetically controlled, and the rate constant is established.

The successful application of heterogeneous catalysts for the preparation of methyl anthranilate avoids the step of neutralisation of the excess acid used in the conventional methods. The product separation while using solid acids is very easy, and thereby the overall yields are also increased.

The scale-up of this reaction for a mechanically agitated contactor is straightforward, wherein the same tip speed would be a criterion. The catalyst cost on the basis of laboratory experiments with minimum 5 times recycle turns out to be less than 2.3% of the product cost, which is economical. We can compare this with a typical sulphuric acid based process for which the cost is 1% including the cost of neutralisation of the liquid acid. However, the corrosion and treatment of salt generated after neutralisation of the liquid acid would be much greater. Thus, this ecofriendly process is definitely economically viable.

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